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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/564,010	01/11/2006	Richard Anthony Borman	224822/PO18 US/127425	8896

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EXAMINER

RAO, SAVITHA M

ART UNIT	PAPER NUMBER
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1614

MAIL DATE	DELIVERY MODE
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03/16/2010

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/564,010	Applicant(s) BORMAN ET AL.	
	Examiner SAVITHA RAO	Art Unit 1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 November 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 92-97 and 99-119 is/are pending in the application.
- 4a) Of the above claim(s) 92-95, 99-115 and 117-119 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 96, 97 and 116 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 92-97 and 99-119 are pending .

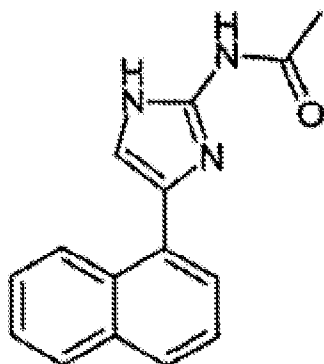
Receipt and consideration of Applicants' amended claim set and remarks/arguments filed on 11/24/2009 is acknowledged. New claims 115-119 are added. Claims 92-95, 99-115 and 117-119 are withdrawn from consideration as being drawn to non-elected invention and specie. Claims under consideration in the instant office action are claims 96-97 and 116.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/24/2009 has been entered.

Applicants' arguments, filed 11/23/2009, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Election by original presentation:

Newly added claims 115 and 117--119 are directed to a specie which is different from the specie originally elected by the applicant:. In the response to election/restriction dated 10/03/2008 filed by the applicants, applicant elected the following specie (103N from page 97 of the instant disclosure)



Applicant has received an action on the merits for the originally elected specie in the non-final action dated 10/31/2008. However, amendment to instant claim 96 filed on 02/24/2009 did not encompass the original compound (103N from page 97 of the instant disclosure) elected by the applicant. In the final action dated 06/24/2009, the search was therefore extended to the following compound encompassed by the amended claim.

Claims under consideration in the instant office action are claims 96-97 and 116.

Claim Rejections - 35 USC § 103

New grounds of rejection

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

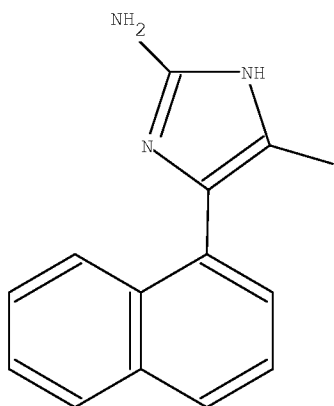
The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

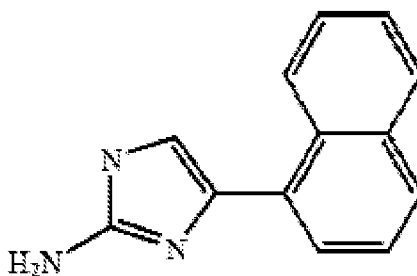
Claims 96-97 and 116 are rejected under 35 U.S.C. 103(a) as being unpatentable over Doweyko et al (US 2006/0223110, reference already of record)

Instant claims are drawn towards the following compound (Extended specie from the compounds encompassed in instant claim 96)



Doweyko et al teaches the following compound (2e) including its synthetic procedure (see structure below) (page 29, section [0320] to be used as an intermediate in the synthesis of compounds useful as modulator of nuclear receptor hormone.

2e



The only difference between the compound taught by Doweyko and the instantly claimed compounds encompassed by the generic formula of instant claim 96 is the

Art Unit: 1614

substitution in the imidazole ring, instead of H in position 5 of the imidazole ring as taught by Doweyko, instant claims recite substitution of a C1-6 alkyl, C3-7 cycloalkyl etc group in addition to the naphthyl and amine substituents. With regards to the H v. -CH₃ substitution, Hydrogen and methyl are deemed obvious variants. In re Wood, 199 USPQ 137 (CCPA 1978), and In re Lohr, 137 USPQ 548,549 (CCPA 1963) and the interchange of alkyl and hydrogen is obvious in and of itself, Ex parte Blustone 135, USPQ 199.

MPEP 2144.08.II.A.4(c) states, "... consider teachings of a preferred species within the genus. If such a species is structurally similar to that claimed, its disclosure may motivate one of ordinary skill in the art to choose the claimed species or subgenus from the genus, based on the reasonable expectation that structurally similar species usually have similar properties." To those skilled in the chemical art, one homologue is not an advance over an adjacent member of a homologous series. The reason for this is that one of ordinary skill, knowing the properties of one member of series, would know what properties to expect in adjacent members USPQ 137. Accordingly, it would have been obvious for one of ordinary skill in the art to substitute methyl group for the hydrogen group in the imidazole ring.

The differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. A person of ordinary skill in the art would have been motivated to further modify the compounds disclosed by Doweyko et. al. to add a methyl substitution

Art Unit: 1614

instead of H on the imidazole ring. The instantly claimed compounds read on structural homologs of the reference compounds. Hydrogen and methyl are adjacent homologue. Accordingly, one having ordinary skill in the art would have been motivated to prepare the instantly claimed compound because such structurally homologous compounds are expected to possess similar properties. To those skilled in chemical art, one homologue is not such an advance over adjacent member of series as requires invention because chemists knowing properties of one member of series would in general know what to expect in adjacent members. *In re Henze*, 85 USPQ 261 (1950). . Therefore, the unsubstituted position comprising the hydrogen moiety in the imidazole structure adequately suggests to the pharmaceutical a possible methyl group on the imidazole structure. Therefore, the claims are *prima facie* obvious over the prior art. It is also noted that has been held that compounds that are structurally homologous to prior art compounds are *prima facie* obvious, absent a showing of unexpected results. *In re Hass*, 60 USPQ 544 (CCPA 1944);

Response to applicant's arguments filed on 11/24/2009 :

Applicant traverses the above rejection with the following arguments:

- a. That one of skill in the art looking to develop antagonists of the 5-HT_{2B} receptor would not choose to modify the intermediate compounds of Doweyko which are used for the synthesis of compounds to be tested for binding to Nuclear Hormone Receptor site
- II. Doweyko does not teach that these compounds have any pharmacological activity.

Art Unit: 1614

b. Applicant's further argue that the in re woods does not stand for the proposition that hydrogen and methyl are equivalent in all cases.

Applicant's traversal arguments for this rejection have been fully considered, but are not found to be persuasive.

It is noted that the instant claims 96-97 are drawn to a compound and not to a method of treatment. Accordingly, Doweyko provides a compound structurally similar to the instantly claimed compounds without a methyl substituent on the imidazole ring as shown in the above rejection. Doweyko teaches this compounds as an intermediate in the preparation of compounds which possess Nuclear Hormone Receptor site binding properties. As such, the instant compounds are shown to have utility in the preparation of compounds which are useful as modulators of nuclear receptor hormones.

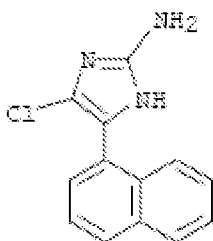
With respect to applicant's arguments against In-re wood, while the molecule on which the In-re wood decision was based is not the same as the instantly claimed, the general teachings of In-re wood that substitution of H instead of methyl is obvious applies to the instant case. As noted above, an ordinarily skilled artisan would be motivated to make this substitution with a reasonable expectation of retaining the property of the original compound.

Accordingly, the arguments set forth by the applicant are unpersuasive and the rejection is maintained.

Claims 96-97 and 116 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nath et al. (Indian Journal of Chemistry, 1980, volume 19B,

pages 536-538, abstract) in view of Patani et al. (Chemical Reviews, 1996, volume 96, pages 3147-3176, reference already of record).

Nath et al teaches the following substituted imidazole
1H-imidazol-2-amine, 5-chloro-4-(1-naphthalenyl) (1-naphthalenyl)



Nath et al. additionally teaches that both halogenated and nonhalogenated imidazoles exhibits antifungal activity against *piricularia ocyzae* and antibacterial activity against the common pathogenic bacteria, *S.Aureas* and *E.Coli* (see abstract).

The only difference between the instantly claimed compound and above compound taught by Nath et al. is the Chlorine substitution on position 5 of the imidazole ring instead of the methyl group.

However, Patani et al teaches that the Cl group and CH₃ group are bioisosteres and one can be substituted by the other without any loss or change in activity. Patani teaches as an extension of the Grimm's hydride displacement law (Fluorine and Hydroxyl, amino or methyl groups are bioisosteres) there is widespread use of chlorine atom as the bioisosteres in several different series of biologically active compounds and attributes it to the similarity in size between these atoms. Patani et al further teaches that there exists similarity in the lipophilicity of the methyl group with that of chlorine which may be responsible for its suitability as a monovalent bioisosteric replacement

Art Unit: 1614

(page 3153, left column, 2nd paragraph). Patani teaches an evaluation study of compounds as novel potassium channel openers wherein replacement of chlorine with isosteres of Grimm's hydride displacement law (CH_3 and NH_2) (see Table 11, page 3153) wherein substitution of chlorine with CH_3 results in analogues with similar biological activity (page 3153, left col., 3rd paragraph).

Accordingly, it would have been *prima facie* obvious to the skilled artisan to synthesize the instantly claimed compounds. Instantly claimed compound with a methyl substitution on the naphthyl ring instead of chlorine already taught in the art. In view of the close structural similarity between the claimed compound in the instant and the compound taught by Nath et al. one of ordinary skilled in the art would have been motivated to formulate instantly claimed compounds, substituting the Chlorine group in Nath et al.'s compounds with methyl group motivated from Patani's teachings that chlorine and methyl group are bioisosteres. There would be a reasonable expectation of success that the substituted compound would have the same properties and function as that of the compounds taught by Nath et al which is antifungal and antibacterial activity since the compounds have similar structures. A *prima facie* case of obviousness may be made when chemical compounds have very close structural similarities and/or similar utilities. "An obviousness rejection based on similarity in chemical structure and/or function entails the motivation of one skilled in the art to make a claimed compound, in the expectation that compounds similar in structure will have similar properties." *In re Payne*, 606 F.2d 303, 313, 203 USPQ 245, 254 (CCPA 1979). See *In*

Art Unit: 1614

re Papesch, 315 F.2d 381, 137 USPQ 43 (CCPA 1963) and In re Dillon, 919 F.2d 688, 16 USPQ2d 1897 (Fed. Cir. 1991).

Conclusion

Claims 96-97 and 116 are rejected. No claims are allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAVITHA RAO whose telephone number is (571)270-5315. The examiner can normally be reached on Mon-Fri 7 am to 4 pm..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached at 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Application/Control Number: 10/564,010

Page 13

Art Unit: 1614

/SAVITHA RAO/

Examiner, Art Unit 1614

/Ardin Marschel/

Supervisory Patent Examiner, Art Unit 1614